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<110>   Biotica Technology Limited
        Pfizer Inc
        Gaisser, Sabine

<120>   Polyketides and their synthesis

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<150>   GB0327721.7
<151>   2003-11-28

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<170>   PatentIn version 3.2

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Leu Met Leu Ala Gly Ile Arg Glu Ile Gln Ile Ile Ser Ser Lys Asp
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His Leu Asp Leu Phe Arg Ser Leu Leu Gly Glu Gly Asp Arg Leu Gly
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Leu Ser Ile Ser Tyr Ala Glu Gln Arg Glu Pro Arg Gly Ile Ala Glu
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Ile Leu Gly Asp Asn Val Phe His Gly Pro Gly Phe Ser Ser Val Leu
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     Ala Cys Ile Glu Glu Ile Ala Met Arg Met Gly Phe Ile Ser Ala Glu
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Leu Ser Ile Ser Tyr Ala Glu Gln Arg Glu Pro Arg Gly Ile Ala Glu
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Ile Leu Gly Asp Asn Val Phe His Gly Pro Gly Phe Ser Ser Val Leu
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Val Lys Asp Ala His Arg Tyr Gly Val Gly Glu Ile Asp Ser Gly Gly
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Arg Leu Leu Ser Leu Glu Glu Lys Pro Arg Arg Pro Leu Glu Pro Gly
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Thr Val Val Leu Asp Lys Leu Thr Tyr Ala Gly Asn Pro Ala Asn Leu
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Glu His Val Ala Gly His Pro Asp Leu Glu Phe Val Arg Gly Asp Ile
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Ala Asp Gln Ala Leu Val Arg Arg Leu Met Glu Gly Val Gly Leu Val
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Val His Phe Ala Ala Glu Ser His Val Asp Arg Ser Ile Glu Ser Ser
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Glu Ala Phe Val Arg Thr Asn Val Glu Gly Thr Arg Val Leu Leu Gln
                100   105   110

Ala Ala Val Asp Ala Gly Val Gly Arg Phe Val His Ile Ser Thr Asp
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Glu Val Tyr Gly Ser Ile Ala Glu Gly Ser Trp Pro Glu Asp His Pro
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Leu Ala Leu Ala Tyr His Arg Thr Tyr Gly Leu Asp Val Arg Val Thr
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Arg Cys Ser Asn Asn Tyr Gly Pro Arg Gln Tyr Pro Glu Lys Ala Val
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Pro Leu Phe Thr Thr Asn Leu Leu Asp Gly Leu Pro Val Pro Leu Tyr
                195   200   205

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Ile Leu Glu Leu Cys Gly Ala Asp Arg Ser Ala Val Arg Arg Val Ala
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Asp Arg Pro Gly His Asp Arg Arg Tyr Ser Val Asp Thr Thr Lys Ile
        275             280             285

Arg Glu Glu Leu Gly Tyr Ala Pro Arg Thr Gly Ile Thr Glu Gly Leu
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Thr Val Val Leu Asp Lys Leu Thr Tyr Ala Gly Asn Pro Ala Asn Leu
            35              40              45

Glu His Val Ala Gly His Pro Asp Leu Glu Phe Val Arg Gly Asp Ile
    50              55              60

Ala Asp His Gly Trp Trp Arg Arg Leu Met Glu Gly Val Gly Leu Val
65              70              75              80
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Val His Phe Ala Ala Glu Ser His Val Asp Arg Ser Ile Glu Ser Ser
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5   Glu Ala Phe Val Arg Thr Asn Val Glu Gly Thr Arg Val Leu Leu Gln
                    100   105   110

10   Ala Ala Val Asp Ala Gly Val Gly Arg Phe Val His Ile Ser Thr Asp
                    115   120   125

15   Glu Val Tyr Gly Ser Ile Ala Glu Gly Ser Trp Pro Glu Asp His Pro
                    130   135   140

     Val Ala Pro Asn Ser Pro Tyr Ala Ala Thr Lys Ala Ala Ser Asp Leu
     145   150   155   160

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25   Arg Cys Ser Asn Asn Tyr Gly Pro Arg Gln Tyr Pro Glu Lys Ala Val
                    180   185   190

30   Pro Leu Phe Thr Thr Asn Leu Leu Asp Gly Leu Pro Val Pro Leu Tyr
                    195   200   205

35   Gly Asp Gly Gly Asn Thr Arg Glu Trp Leu His Val Asp Asp His Cys
         210   215   220

     Arg Gly Val Ala Leu Val Gly Ala Gly Gly Arg Pro Gly Val Ile Tyr
     225   230   235   240

40   Asn Ile Gly Gly Gly Thr Glu Leu Thr Asn Ala Glu Leu Thr Asp Arg
                    245   250   255

45   Ile Leu Glu Leu Cys Gly Ala Asp Arg Ser Ala Leu Arg Arg Val Ala
                    260   265   270

50   Asp Arg Pro Gly His Asp Arg Arg Tyr Ser Val Asp Thr Thr Lys Ile
                    275   280   285

55   Arg Glu Glu Leu Gly Tyr Ala Pro Arg Thr Gly Ile Thr Glu Gly Leu
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cacgcccggc tgctgtgggg tcccgacgtg gtcctcaacg cacggcggca gttcacccgg    1860

ctgctcgccg agcgccccgt cgaacagcgc gaggacccgg tcggcgaatg gctcacgtgg    1920

acgctggagc gccacggcct cgccgccgac gcggacacga tcgaggaact gttcgccggg    1980

cagtggacga tcgaccccag cgccgggagc ctgcggctgc cggtcgacgg cgaggtcgtg    2040

cccatgcgct tcgtgccgta caacggcgcc tcggtcgtcc cgcctggct ctccgagccg     2100

cctgcccggc cccgggtctg cgtcaccctc ggcgtctcca cccgggagac ctacggcacg    2160

gacggcgtcc cgttccacga actgctggcc ggactggccg acgtggacgc cgagatcgtc    2220

gccaccctcg acgcggggca gctcccggac gccgccggtc tgcccggcaa tgtgcgcgtc    2280.

gtcgacttcg tgccgctgga cgccctgctg ccgagctgcg ccgcgatcgt ccaccacgga    2340

ggcgcgggaa cctgtttcac ggccaccgtg cacggcgtcc cgcagatcgt cgtggcctcc    2400

ctctgggacg cgccgctgaa ggcgcaccaa ctcgccgagg cgggcgccgg gatcgccctg    2460

gaccccgggg aactgggcgt ggacaccctg cgcggcgccg tcgtgcgggt gctggagagc    2520

cgcgagatgg ccgtggcggc gcgtcgcctc gccgacgaga tgctcgccgc ccccaccccg    2580

gccgcgctcg tcccccgcct cgaacgcctc accgccgcgc accgccgcgc ctgatcccgc    2640

caaggagccc ccatgaacct cgaatacagc ggcgacatcg cccggttgta cgacctggtc    2700

caccagggaa agggcaagga ctaccgggcg gaggccgagg agctggccgc gcttgtcacc    2760

cagcgccgcc ccggggcccg ctccctcctc gacgtggcct gcggaacggg gatgcacctg    2820

cggcacctcg gcgacctctt cgaggaggtg gccggggtgg agatgtcccc cgacatgctg    2880

gccatcgcgc agcggcgcaa cccggaggcc ggcatccacc gggggggacat gcgggacttc   2940

gccctcggcc gccgcttcga cgccgtgatc tgcatgttca gttccatcgg gcacatgcgc    3000

gaccagcggg aactggacgc ggcgatcggc cggttcgccg cgcacctgcc gtccggcggg    3060

gtcgtgatcg tcgatccctg gtggttcccg gagacgttca caccggggta cgtcggcgcg    3120

agcctcgtcg aggccgaggg ccgcaccatc gcgcgcttct cccactccgc gctcgaggac    3180

ggcgcgaccc ggatcgatgt ggactacctc gtcggcgtgc cggggggaggg ggtgcggcac    3240

ttgaaggaga cccatcggat cacgcttttc gggcgtgcgc agtacgaggc ggccttcacc    3300

gcggcgggga tgtccgtcga gtacctcccg cacgccgcca ccgaccgcgg actcttcgtc    3360

ggcgtccagg cctga                                                     3375
```

```
        Met Lys Gly Ile Ile  Leu Ala Gly Gly Ser  Gly Thr Arg Leu Arg  Pro
        1               5                    10                  15

 5
        Leu Thr Gly Ala Leu  Ser Lys Gln Leu Leu  Pro Val Tyr Asp Lys  Pro
                    20                   25                  30

10
        Met Ile Tyr Tyr Pro  Leu Ser Val Leu Met  Leu Ala Gly Ile Arg  Asp
                    35                   40                  45

        Ile Gln Ile Ile Thr  Ser Lys Thr His Leu  Glu Met Phe Arg Ser  Leu
15          50                   55                  60

        Leu Gly Asp Gly Ser  Arg Ile Gly Ile Ser  Val Gly Tyr Ala Glu  Gln
            65                   70                  75                  80

20
        Glu Glu Pro Arg Gly  Ile Ala Glu Ala Phe  Leu Ile Gly Glu Glu  His
                    85                   90                  95

25
        Ile Gly Asp Asp Pro  Val Ala Leu Ile Leu  Gly Asp Asn Val Phe  His
                    100                  105                 110

30
        Gly Pro Gly Phe Ser  Ser Val Leu Ala Ser  Thr Ala Ala Arg Leu  Asp
                    115                  120                 125

        Gly Cys Glu Leu Phe  Gly Tyr Pro Val Lys  Asp Pro Arg Arg Tyr  Gly
35          130                  135                 140

        Val Gly Glu Val Asp  Ala Glu Gly Arg Leu  Val Ser Leu Glu Glu  Lys
            145                  150                 155                 160

40
        Pro Glu Lys Pro Arg  Ser His Leu Ala Val  Thr Gly Leu Tyr Phe  Tyr
                    165                  170                 175

45
        Asp Asn Gly Val Val  Asp Ile Ala Arg Arg  Leu Thr Pro Ser Pro  Arg
                    180                  185                 190

50
        Gly Glu Leu Glu Ile  Thr Asp Val Asn Lys  Val Tyr Leu Glu Gln  Gly
                    195                  200                 205

        Arg Ala Arg Met Thr  Glu Leu Gly Arg Gly  Phe Ala Trp Leu Asp  Met
55          210                  215                 220

        Gly Thr His Ser Ser  Leu Leu Gln Ala Gly  Gln Tyr Val Gln Leu  Leu
            225                  230                 235                 240
50
```

Glu Gln Arg Gln Gly Val Arg Ile Ser Cys Val Glu Glu Ile Ala Leu
            245   250   255

Arg Met Gly Tyr Ile Ser Ala Arg Gln Cys His Glu Leu Gly Arg Glu
            260   265   270

Leu Glu Ser Ser Ser Tyr Gly Arg Tyr Leu Met Asp Val Ala Glu Thr
        275   280   285

Leu Met Ser Gly Pro Ala Ala
        290   295

<210> 9
<211> 332
<212> PRT
<213> Streptomyces eurythermus

<400> 9

Met Arg Leu Leu Val Thr Gly Gly Ala Gly Phe Ile Gly Ser His Phe
1   5   10   15

Val Arg Gln Leu Leu Ala Gly Ala Tyr Pro Asp Leu Ala Gly Ala Arg
            20   25   30

Thr Val Val Val Asp Lys Leu Thr Tyr Ala Gly Asn Leu Ala Asn Leu
        35   40   45

Asp Pro Val Ala Asp His Pro Ser Leu Glu Phe Val His Ala Asp Ile
        50   55   60

Arg Asp Ala Glu Val Met Ser Arg Val Val Arg Gly Ala Asp Val Val
65   70   75   80

Val His Phe Ala Ala Glu Ser His Val Asp Arg Ser Ile Ala Asp Ala
                85   90   95

Ser Ala Phe Val Glu Thr Asn Val Arg Gly Thr Gln Val Leu Leu Gln
            100   105   110

Ala Ala Val Glu Ala Gly Ala Gly Arg Phe Val His Val Ser Thr Asp
        115   120   125

Glu Val Tyr Gly Ser Ile Ala Glu Gly Ser Trp Arg Glu Glu Gln Pro
        130   135   140

Leu Ala Pro Asn Ser Pro Tyr Ala Ala Ser Lys Ala Ala Ser Asp Leu
145   150   155   160

Leu Ala Leu Ala Tyr His Arg Thr Tyr Gly Leu Pro Val Val Val Thr
                165   170   175

Arg Cys Ser Asn Asn Tyr Gly Pro Tyr Gln His Pro Glu Lys Val Val
            180   185   190

Pro Leu Phe Ala Thr Asn Leu Leu Asp Gly Leu Thr Val Pro Leu Tyr
        195   200   205

Ser Asp Gly Gly Asn Ser Arg Asp Trp Leu His Val Asp Asp His Cys
        210   215   220

Arg Gly Ile Ser Leu Val Ala Thr Arg Gly Arg Pro Gly Glu Val Tyr
225   230   235   240

His Ile Gly Gly Gly Thr Glu Leu Thr Asn Arg Glu Leu Thr Lys Arg
                245   250   255

Leu Leu Gly Leu Cys Gly Ala Asp Ala Ser Ser Val Arg His Val Ala
        260   265   270

Asp Arg Pro Gly His Asp Leu Arg Tyr Ala Leu Asp Ile Gly Lys Ile
        275   280   285

Thr Gly Glu Leu Gly Tyr Ala Pro Arg Thr Asp Phe Thr Thr Gly Leu
    290   295   300

Ala Asp Thr Val Arg Trp Tyr Ala Glu Asn Arg Ala Trp Trp Glu Pro
305   310   315   320

Leu Lys Lys Ala Ala Gln Glu Ala Arg Arg Thr Asp
                325   330

<210> 10
<211> 787
<212> PRT
<213> Streptomyces eurythermus

<400> 10

Val Ser Thr Pro Ser Ala Pro Pro Val Pro Gly Ala Pro Ser Pro Ala
1   5   10   15

Gly His Pro Asp Glu Gly Leu Trp Val Arg Arg Tyr Arg Pro Val Arg
                20   25   30

```
     Asp Pro Glu Leu Arg Leu Val Cys Phe Pro His Ala Gly Gly Ala Ala
             35              40          45

5    Thr Ser Phe Ala Ala Leu Ala Arg Gly Leu Asp Glu Thr Val Glu Ala
             50              55          60

10   Leu Ala Val Gln Tyr Pro Gly Arg Gln Asp Arg Arg His Glu Pro Phe
         65          70              75              80

     Ile Pro Ser Ile Ser Gly Leu Val Asp Gln Val Val Pro Glu Ile Leu
15                   85              90              95

     Arg Trp Ala Asp Arg Pro Leu Ala Leu Phe Gly His Ser Met Gly Ala
                 100             105             110
20

     Thr Val Ala Phe Glu Val Ala Arg Arg Leu Arg Gly Ser Gly Gln Ala
                 115             120             125

25   Ser Pro Val His Leu Leu Val Ser Gly Arg Arg Ala Pro Thr Val Arg
         130             135             140

     Arg Arg Asp Val Ala His Leu Leu Asp Asp Asp Ala Leu Ile Ala Glu
30   145             150             155             160

     Ile Ala Thr Leu Gln Gly Thr Glu Asp Ala Val Leu Gln Asp Glu Glu
                 165             170             175
35

     Leu Leu Arg Leu Ala Leu Pro Ala Ile Arg Asn Asp Tyr Arg Ala Ala
                 180             185             190
40

     Gly Thr Tyr Ala Tyr Val Pro Gly Gly Ala Leu Asp Cys Pro Val Thr
             195             200             205

45   Val Leu Thr Gly Asp Arg Asp Pro Asp Val Pro Leu Glu Glu Ala Arg
         210             215             220

     Ala Trp Arg Glu Leu Thr Thr Gly Pro Phe Ala Leu His Thr Phe Ala
50   225             230             235             240

     Gly Gly His Phe Tyr Leu Asn Asp Arg Met Asp Glu Val Cys Arg Thr
                 245             250             255
55

     Ile Gly Asp Ala Leu Ala Gly Thr Ala Thr Ala Asp Thr Ala Thr Gly
                 260             265             270

50   Thr Val Pro Pro Arg Thr Ala Ala Asp Thr Ser Thr Gly Pro Val Pro
```

```
                 275                      280                     285

 5    Pro Arg Thr Ala Ala Asp Thr Ala Arg Glu Pro Val Pro Pro Arg Ser
          290              295              300

      Ala Pro Ala Pro His Gly Ala Ala Arg Arg Arg Ala Asp Ala Val Arg
10    305              310              315              320

      Pro Gly Asp Pro Val Asp Thr Ala Arg Arg Val Leu Val Ser Ala Arg
                      325              330              335

15    Thr Ala Asp Ser Ala Val Thr Pro Phe Asp Gly Ile Ser Gly Trp Leu
                  340              345              350

20    Ala Glu Arg Leu Arg Ala Gly Arg Phe Asp Val Ser Arg Val Pro Phe
              355              360              365

      Ala Glu Leu Arg Gly Trp Ser Phe His Pro Gly Thr Gly Asn Leu His
25        370              375              380

      His Ala Ser Gly Arg Phe Phe Ser Val Glu Gly Leu His Val Arg Thr
      385              390              395              400
30
      Asp Arg Leu Pro Glu Arg Gly Trp Thr Gln Pro Ile Ile Val Gln Pro
              ·       405              410              415
35
      Glu Val Gly Leu Leu Gly Ile Val Ala Arg Glu Ile Asp Gly Val Leu
                  420              425              430

40    His Phe Leu Met Gln Ala Lys Met Glu Pro Gly Asn Val Asn Val Leu
              435              440              445

      Gln Val Ser Pro Thr Val Gln Ala Thr Arg Ser Asn Phe Thr Gly Val
45        450              455              460

      His Arg Gly Arg Asp Ile Arg Tyr Leu Asp Leu Phe Met Gly Pro Arg
      465              470              475              480
50
      Arg Ala Arg Val Leu Val Asp Ser Ile Gln Ser Glu Gln Ala Asp Trp
                  485              490              495
55
      Phe Leu Ala Lys Arg Asn Arg Asn Met Ile Val Glu Leu Ala Ala Asp
              500              505              510

60    Asp Asp Leu Asp Ile Gly Glu Asp Phe Arg Trp Leu Thr Leu Gly Gln
              515              520              525
```

Leu Arg Arg Leu Leu Met Leu Asp Asn Val Val Asn Met Asp Ala Arg
    530   535   540

Ser Ile Leu Ala Cys Leu Pro Thr Ala Asp Ala Asp Ala Ser Ala Pro
545   550   555   560

Ser Pro Val Leu Arg Ser Phe Phe Gly Ser Pro Gly Ala Ala Arg His
            565   570   575

Thr Thr Ala Glu Val Leu Thr Trp Phe Thr Gly Val Arg Ala Leu Arg
            580   585   590

Glu Leu Val Gln Asn Arg Val Pro Leu Asp Thr Val Thr Ala Asp Gly
        595   600   605

Trp Tyr Arg Thr Pro His Glu Ile Ala His Glu Ser Gly Arg His Phe
    610   615   620

Arg Val Met Ala Ala Glu Val Ser Ala Ser Ser Arg Glu Val Thr Ser
625   630   635   640

Trp Thr Gln Pro Leu Ile Glu Pro Arg Leu Pro Gly Leu Met Ala Leu
            645   650   655

Leu Val Lys Ser Val Asp Gly Val Leu His Ala Leu Val Arg Ala Arg
            660   665   670

Val Asp Val Gly His Leu Asn Val Ala Glu Leu Ala Pro Thr Val Gln
        675   680   685

Cys Arg Pro Gln Glu His Thr Gly Pro Arg Gly Leu Pro Gly Pro Pro
    690   695   700

Tyr Leu Glu Asp Val Leu Ser Ala Pro Pro Gln Asp Val Arg Tyr Asp
705   710   715   720

Ala Val Gln Ser Glu Glu Gly Gly Arg Phe Phe His Ala Gln Asn Arg
            725   730   735

Tyr Val Ile Val Glu Val Pro His Asp Phe Pro Glu Asp Ala Pro Asp
            740   745   750

Asp Phe Ala Trp Leu Ser Leu Gly Gln Leu Thr Gly Leu Leu Ala His
    755   760   765

```
Gly Asn Tyr Leu Asn Ile Glu Leu Arg Thr Leu Val Ala Cys Ala His
    770             775             780
```

```
Thr Leu Tyr
785
```

```
<210>  11
<211>  333
<212>  PRT
<213>  Streptomyces eurythermus
```

```
<400>  11
```

```
Met Val Asn Asp Pro Met Pro Arg Gly Ser Gly Ser Gly Ser Val Val
1               5               10              15
```

```
Val Leu Gly Gly Ala Gly Tyr Val Gly Arg His Val Cys Ala Ala Phe
            20              25              30
```

```
Ala Ala Arg Gly Arg Asp Val Val Val Gly Arg Arg Pro Pro Glu
        35              40              45
```

```
Glu Pro Met Pro Tyr Arg Cys Val Thr Leu Asp Leu Ala Gly Thr Asp
    50              55              60
```

```
Pro Ala Ala Leu Ala Ala Ala Leu Asp Ala Glu Arg Pro Asp Thr Ile
65              70              75              80
```

```
Val Asn Ser Val Gly Ser Ile Trp Gly Arg Thr Asp Glu Gln Met Trp
                85              90              95
```

```
Ser Ala Thr Ala Val Pro Thr Leu Arg Leu Leu Glu Ala Leu Ala Leu
            100             105             110
```

```
Met Ser Ala Arg Pro Arg Leu Val His Leu Gly Ser Val Leu Glu Tyr
        115             120             125
```

```
Gly Pro Val Thr Pro Gly Gly Ser Val Gly Ala Asp Ala Val Pro Arg
        130             135             140
```

```
Pro Asp Thr Ala Tyr Gly Arg Ser Lys Leu Ala Ala Ser Glu Ala Val
145             150             155             160
```

```
Leu Arg Gly Thr Ser Gly Gly Trp Val Asp Gly Val Val Leu Arg Val
            165             170             175
```

```
Ser Asn Val Ser Gly Pro Gly Thr Pro Arg Ile Ser Leu Leu Gly Gln
```

                    180   185   190

5   Val Ala Glu Arg Leu Leu Ala Ala Ala Gly Thr Gly Ala Glu Ala Val
                195   200   205

         Val Glu Leu Ser Arg Leu Arg Ala His Arg Asp Tyr Val Asp Val Arg
                210   215   220
10

         Asp Val Ala Asp Ala Val Val Ala Ala Ala Arg Ala Pro Ala Val Pro
         225   230   235   240

15
         Val Ala Val Gly Ile Gly Arg Gly Glu Ala Val Ala Val Arg Asp Leu
                        245   250   255

20   Val Gly Leu Phe Ile Glu Ala Ser Gly Ile Pro Ala Arg Val Val Glu
                        260   265   270

         Arg Pro Ala Pro Gly Arg Ala Pro Gly His Arg Glu Asp Trp Leu Arg
                275   280   285
25

         Val Asp Thr Gly Ala Ala Arg Ala Leu Leu Gly Trp Ala Pro Arg Arg
                290   295   300
30

         Ser Leu Arg Glu Ser Val Arg Asp Cys Trp His Asp Leu Val Arg Ala
         305   310   315   320

35
         His Arg Leu Pro Thr Thr Pro Ser Lys His Ser Gly Gly
                        325   330

40   <210> 12
         <211> 373
         <212> PRT
         <213> Streptomyces eurythermus

45   <400> 12

         Val Thr Thr Tyr Val Trp Asp Tyr Leu Ala Glu Tyr Gln Asn Glu Arg
         1   5   10   15

50
         Ala Asp Leu Leu Asp Ala Val Glu Thr Val Phe Ala Ser Gly Gln Leu
                        20   25   30

55   Val Leu Gly Pro Ser Val Asp Gly Phe Glu Lys Glu Phe Ala Asp Tyr
                        35   40   45

         His Gly Leu Arg His Cys Gly Gly Val Asp Asn Gly Thr Asn Ala Val
50   50   55   60

```
        Lys Leu Gly Leu Gln Ala Leu Gly Val Gly Pro Gly Asp Glu Val Val
        65              70              75              80

        Thr Val Ser Asn Thr Ala Ala Pro Thr Val Val Ala Ile Asp Gly Thr
                        85              90              95

        Gly Ala Thr Pro Val Phe Val Asp Val Arg Ala Glu Asp His Leu Met
                    100             105             110

        Asp Thr Asp Gln Val Ala Asp Val Ile Thr Pro Arg Thr Lys Ala Leu
                115             120             125

        Leu Pro Val His Leu Tyr Gly Gln Cys Val Asp Met Ala Pro Leu Arg
            130             135             140

        Ala Leu Ala Glu Gln His Gly Leu Val Val Leu Glu Asp Cys Ala Gln
        145             150             155             160

        Ala His Gly Ala Arg His His Gly Glu Leu Ala Gly Thr Leu Gly Asp
                        165             170             175

        Ala Ala Ala Phe Ser Phe Tyr Pro Thr Lys Val Leu Gly Ala Tyr Gly
                    180             185             190

        Asp Gly Gly Ala Val Leu Thr Asp Asp Ala Asp Val Asp Arg Ala Leu
                195             200             205

        Arg Arg Leu Arg Tyr Tyr Gly Met Glu Asp Val Tyr Tyr Val Val Gln
            210             215             220

        Thr Pro Gly His Asn Ser Arg Leu Asp Glu Val Gln Ala Glu Ile Leu
        225             230             235             240

        Arg Arg Lys Leu Thr Arg Leu Asp Arg Tyr Ile Glu Gly Arg Arg Ala
                        245             250             255

        Val Ala Arg Arg Tyr Ala Glu Gly Leu Ala Asn Leu Thr Gly Pro Gly
                    260             265             270

        Gly Leu Val Leu Pro Ser Val Thr Glu Gly Asn Asp His Val Tyr Tyr
                275             280             285

        Val Tyr Val Val Arg His Pro Arg Arg Asp Asp Ile Ile Glu Ala Leu
            290             295             300
```

```
Lys Ser Tyr Gly Ile Ser Leu Asn Ile Ser Tyr Pro Trp Pro Val His
305             310             315             320


Thr Met Thr Gly Phe Ala His Leu Gly Tyr Ala Lys Gly Ser Leu Pro
                325             330             335


Val Thr Glu Arg Leu Ala Asp Glu Ile Phe Ser Leu Pro Met Tyr Pro
            340             345             350


Gly Leu Ala Pro Asp Val Gln Asp Lys Val Ile Ala Ala Leu His Glu
            355             360             365


Val Leu Ala Thr Leu
    370


<210>  13
<211>  447
<212>  PRT
<213>  Streptomyces eurythermus

<400>  13

Val Ser Pro Ala Pro Ala Thr Glu Asp Pro Ala Ala Ala Gly Arg Arg
1               5               10              15


Leu Gln Leu Thr Arg Ala Ala Gln Trp Phe Ala Gly Thr Gln Asp Asp
            20              25              30


Pro Tyr Ala Leu Val Leu Arg Ala Glu Ala Thr Asp Pro Ala Pro Tyr
        35              40              45


Glu Glu Arg Ile Arg Ala His Gly Pro Leu Phe Arg Ser Asp Leu Leu
    50              55              60


Asp Thr Trp Val Thr Ala Ser Arg Ala Val Ala Asp Glu Val Ile Thr
65              70              75              80


Ser Pro Ala Phe Asp Gly Leu Thr Ala Asp Gly Arg Arg Pro Gly Ala
                85              90              95


Arg Glu Leu Pro Leu Ser Gly Thr Ala Leu Asp Ala Asp Arg Ala Thr
            100             105             110


Cys Ala Arg Phe Gly Ala Leu Thr Ala Trp Gly Gly Pro Leu Leu Pro
            115             120             125


Ala Pro His Glu Arg Ala Leu Arg Glu Ser Ala Glu Arg Arg Ala His
    130             135             140
```

```
     Thr Leu Leu Asp Gly Ala Glu Ala Ala Leu Ala Ala Asp Gly Thr Val
     145             150             155             160

     Asp Leu Val Asp Ala Tyr Ala Arg Arg Leu Pro Ala Leu Val Leu Arg
                     165             170             175

     Glu Gln Leu Gly Val Pro Glu Glu Ala Ala Thr Ala Phe Glu Asp Ala
                 180             185             190

     Leu Ala Gly Cys Arg Arg Thr Leu Asp Gly Ala Leu Cys Pro Gln Leu
                 195             200             205

     Leu Pro Asp Ala Val Ala Gly Val Arg Ala Glu Ala Ala Leu Thr Ala
         210             215             220

     Val Leu Ala Ser Ala Leu Arg Gly Thr Pro Ala Gly Arg Ala Pro Asp
     225             230             235             240

     Ala Val Ala Ala Ala Arg Thr Leu Ala Val Ala Ala Ala Glu Pro Ala
                     245             250             255

     Ala Thr Leu Val Gly Asn Ala Val Gln Glu Leu Leu Ala Arg Pro Ala
                 260             265             270

     Gln Trp Ala Glu Leu Val Arg Asp Pro Arg Leu Ala Ala Ala Ala Val
                 275             280             285

     Thr Glu Thr Leu Arg Val Ala Pro Pro Val Arg Leu Glu Arg Arg Val
         290             295             300

     Ala Arg Glu Asp Thr Asp Ile Ala Gly Gln Arg Leu Pro Ala Gly Gly
     305             310             315             320

     Ser Val Val Ile Leu Val Ala Ala Val Asn Arg Ala Pro Val Ser Ala
                     325             330             335

     Gly Ser Asp Ala Ser Thr Thr Val Pro His Ala Gly Gly Arg Pro Arg
                 340             345             350

     Thr Ser Ala Pro Ser Val Pro Ser Ala Pro Phe Asp Leu Thr Arg Pro
                 355             360             365

     Val Ala Ala Pro Gly Pro Phe Gly Leu Pro Gly Asp Leu His Phe Arg
         370             375             380
```

Leu Gly Gly Pro Leu Val Gly Thr Val Ala Glu Ala Ala Leu Gly Ala
385   390   395   400

Leu Ala Ala Arg Leu Pro Gly Leu Arg Ala Ala Gly Pro Ala Val Arg
                405   410   415

Arg Arg Arg Ser Pro Val Leu His Gly His Ala Arg Leu Pro Val Ala
                420   425   430

Val Ala Arg Thr Ala Arg Asp Leu Pro Ala Thr Ala Pro Arg Asn
            435   440   445

<210>   14
<211>   424
<212>   PRT
<213>   Streptomyces eurythermus

<400>   14

Met Arg Ile Leu Leu Thr Ser Phe Ala His Asn Thr His Tyr Tyr Asn
1   5   10   15

Leu Val Pro Leu Gly Trp Ala Leu Arg Ala Ala Gly His Asp Val Arg
                20   25   30

Val Ala Ser Gln Pro Ser Leu Thr Gly Thr Ile Thr Gly Ser Gly Leu
            35   40   45

Thr Ala Val Pro Val Gly Asp Asp Thr Ala Ile Val Glu Leu Ile Thr
    50   55   60

Glu Ile Gly Asp Asp Leu Val Leu Tyr Gln Gln Gly Met Asp Phe Val
65   70   75   80

Asp Thr Arg Asp Glu Pro Leu Ser Trp Glu His Ala Leu Gly Gln Gln
                85   90   95

Thr Ile Met Ser Ala Met Cys Phe Ser Pro Leu Asn Gly Asp Ser Thr
            100   105   110

Ile Asp Asp Met Val Ala Leu Ala Arg Ser Trp Lys Pro Asp Leu Val
        115   120   125

Leu Trp Glu Pro Phe Thr Tyr Ala Gly Pro Val Ala Ala His Ala Cys
    130   135   140

Gly Ala Ala His Ala Arg Leu Leu Trp Gly Pro Asp Val Val Leu Asn

```
                  145                         150                    155                         160


      5    Ala Arg Arg Gln Phe Thr Arg Leu Leu Ala Glu Arg Pro Val Glu Gln
                         165                    170              175


           Arg Glu Asp Pro Val Gly Glu Trp Leu Thr Trp Thr Leu Glu Arg His
     10              180                    185              190


           Gly Leu Ala Ala Asp Ala Asp Thr Ile Glu Glu Leu Phe Ala Gly Gln
     15              195                    200              205


           Trp Thr Ile Asp Pro Ser Ala Gly Ser Leu Arg Leu Pro Val Asp Gly
                    210                    215              220


     20    Glu Val Val Pro Met Arg Phe Val Pro Tyr Asn Gly Ala Ser Val Val
           225                    230                    235              240


     25    Pro Ala Trp Leu Ser Glu Pro Pro Ala Arg Pro Arg Val Cys Val Thr
                         245                    250              255


           Leu Gly Val Ser Thr Arg Glu Thr Tyr Gly Thr Asp Gly Val Pro Phe
     30              260                    265              270


           His Glu Leu Leu Ala Gly Leu Ala Asp Val Asp Ala Glu Ile Val Ala
                    275                    280              285


     35    Thr Leu Asp Ala Gly Gln Leu Pro Asp Ala Ala Gly Leu Pro Gly Asn
                290                    295              300


     40    Val Arg Val Val Asp Phe Val Pro Leu Asp Ala Leu Leu Pro Ser Cys
           305                    310                    315              320


     45    Ala Ala Ile Val His His Gly Gly Ala Gly Thr Cys Phe Thr Ala Thr
                         325                    330              335


           Val His Gly Val Pro Gln Ile Val Val Ala Ser Leu Trp Asp Ala Pro
     50              340                    345              350


           Leu Lys Ala His Gln Leu Ala Glu Ala Gly Ala Gly Ile Ala Leu Asp
     55              355                    360              365


           Pro Gly Glu Leu Gly Val Asp Thr Leu Arg Gly Ala Val Val Arg Val
     60              370                    375              380


           Leu Glu Ser Arg Glu Met Ala Val Ala Ala Arg Arg Leu Ala Asp Glu
           385                    390                    395              400
```

```
        Met Leu Ala Ala Pro Thr Pro Ala Ala Leu Val Pro Arg Leu Glu Arg
                    405             410             415

        Leu Thr Ala Ala His Arg Arg Ala
                    420


        <210>  15
        <211>  240
        <212>  PRT
        <213>  Streptomyces eurythermus

        <400>  15

        Met Asn Leu Glu Tyr Ser Gly Asp Ile Ala Arg Leu Tyr Asp Leu Val
        1               5               10              15

        His Gln Gly Lys Gly Lys Asp Tyr Arg Ala Glu Ala Glu Glu Leu Ala
                    20              25              30

        Ala Leu Val Thr Gln Arg Arg Pro Gly Ala Arg Ser Leu Leu Asp Val
                    35              40              45

        Ala Cys Gly Thr Gly Met His Leu Arg His Leu Gly Asp Leu Phe Glu
                50              55              60

        Glu Val Ala Gly Val Glu Met Ser Pro Asp Met Leu Ala Ile Ala Gln
        65              70              75              80

        Arg Arg Asn Pro Glu Ala Gly Ile His Arg Gly Asp Met Arg Asp Phe
                        85              90              95

        Ala Leu Gly Arg Arg Phe Asp Ala Val Ile Cys Met Phe Ser Ser Ile
                    100             105             110

        Gly His Met Arg Asp Gln Arg Glu Leu Asp Ala Ala Ile Gly Arg Phe
                    115             120             125

        Ala Ala His Leu Pro Ser Gly Gly Val Val Ile Val Asp Pro Trp Trp
                    130             135             140

        Phe Pro Glu Thr Phe Thr Pro Gly Tyr Val Gly Ala Ser Leu Val Glu
        145             150             155             160

        Ala Glu Gly Arg Thr Ile Ala Arg Phe Ser His Ser Ala Leu Glu Asp
                        165             170             175
```

```
Gly Ala Thr Arg Ile Asp Val Asp Tyr Leu Val Gly Val Pro Gly Glu
            180                 185             190
```

```
Gly Val Arg His Leu Lys Glu Thr His Arg Ile Thr Leu Phe Gly Arg
        195                 200             205
```

```
Ala Gln Tyr Glu Ala Ala Phe Thr Ala Ala Gly Met Ser Val Glu Tyr
        210                 215             220
```

```
Leu Pro His Ala Ala Thr Asp Arg Gly Leu Phe Val Gly Val Gln Ala
225             230             235             240
```

```
<210>  16
<211>  72
<212>  DNA
<213>  Artificial

<220>
<223>  primer

<400>  16
gggggaattca gatctggtct agaggtcagc cggcgtggcg cgcgtgagt tcctccagtc     60

gcgggacgat ct                                                         72


<210>  17
<211>  38
<212>  DNA
<213>  Artificial

<220>
<223>  Primer

<400>  17
gggcatatga acgaccgtcc ccgccgcgcc atgaaggg                             38


<210>  18
<211>  50
<212>  DNA
<213>  Artificial

<220>
<223>  primer

<400>  18
cccctctaga ggtcactgtg cccggctgtc ggcggcggcc ccgcgcatgg               50


<210>  19
<211>  52
<212>  DNA
<213>  Artificial

<220>
<223>  primer
```

```
<400>  19
cccctctaga ggtcatgcgc gctccagttc cctgccgccc ggggaccgct tg          52
```

```
<210>  20
<211>  81
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